# Translation

### PATENT COOPERATION TRE



## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference			
1513	FOR FURTHER A	ACTION	See Form PCT/IPEA/416
International application No. PCT/JP2003/013259		late (day/month/year) 03 (16.10.2003)	Priority date (day/month/year) 16 October 2002 (16.10.2002)
International Patent Classification (IPC) or n C12Q 1/60, 1/26, 1/32, 1/44, G0	ational classification a	and IPC	
Applicant	<del></del>		<u> </u>
Арричан	KYOWA ME	DEX CO., LTD.	
This report is the international prelin     Authority under Article 35 and trans	ninary examination re mitted to the applican	port, established by this t according to Article 36	International Preliminary Examining 5.
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Box No. II Priority			
Box No. III Non-establishm	nent of opinion with re	gard to novelty, invent	ve step and industrial applicability
Box No. IV Lack of unity o			
Box No. V Reasoned states	ment under Article 35	(2) with regard to novel	ty, inventive step or industrial applicability;
Box No. VI Certain docume	planations supporting	such statement	•
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Date of submission of the demand		Date of completion of	f this report
14 May 2004 (14.05.20	04)	10 Nov	vember 2004 (10.11.2004)
Name and mailing address of the IPEA/JP		Authorized officer	
Facsimile No.		Telephone No.	

#### INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

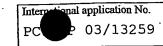
national	application No.	•
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	o. I	Basis of the report	· · ·	013237
1. Wit	th regard	d to the language, this report is based on the international application in the languaged		
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		international search (under Rules 12.3 and 23.1(b))		
		publication of the international application (under Rule 12.4)	•	
		international preliminary examination (under Rules 55.2 and/or 55.3)		
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and	are not	the receiving Office in response to an invitation under Article 14 are referred annexed to this report):	to in this report as "c	riginally filed"
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	made, s (Rule 7	port has been established as if (some of) the amendments annexed to this reportance they have been considered to go beyond the disclosure as filed, as indicated.	t and listed below had cated in the Supplement	d not been
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INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY PCT/JP2003/013259 Box No. IV Lack of unity of invention In response to the invitation to restrict or pay additional fees the applicant has: restricted the claims. paid additional fees. paid additional fees under protest. neither restricted nor paid additional fees. This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees. 3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is complied with. not complied with for the following reasons: See supplemental sheet 4. Consequently, this report has been established in respect of the following parts of the international application: all parts. the parts relating to claims Nos.

#### INTERNATIONAL PECLIMINARY EXAMINATION REPORT



Supplemental Box
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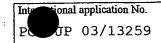
Continuation of: IV. 3.

The inventions set forth in claims 1-10, 12-23 and 25-39 are a group of inventions which address the problem of offering an improved method for simple and accurate measurement of high-density lipoprotein-bound cholesterol, and measurement reagents and kits for the purpose thereof.

By contrast, the inventions set forth in claims 11, 24 and 40-42 are a group of inventions which address the problem of offering compounds described in claim 41.

The two groups of inventions address different problems; therefore, these groups of inventions do not constitute a group of inventions so linked as to form a single general inventive concept.

#### INTERNATIONAL PACLIMINARY EXAMINATION REPORT



v.	Reasoned statement under Article 35(2) with regard to novelty, inventive step or indus	strial applicability;
	citations and explanations supporting such statement	. :

Statement			
Novelty (N)	Claims	2,8-11,15,21-24,26-31,37-42	YES
	Claims	1,3-7,12-14,16-20,25,32-36	NO
Inventive step (IS)	Claims	11, 24, 40-42	YES
	Claims	1-10, 12-23, 25-39	NO
Industrial applicability (IA)	Claims	1-42	YES
	Claims		NO

#### 2. Citations and explanations

Document 1: JP 08-116996 A (Toyobo Co., Ltd.), 14 May 1996

Document 2: WO 97/40376 A1 (Iatron Lab. Inc.), 30 October 1997

Document 3: JP 11-009300 A (Iatron Lab. Inc.), 19 January 1999

Document 4: WO 95/24502 Al (Kyowa Medex Co., Ltd.), 14
September 1995

1. The inventions set forth in claims 1, 3-7, 12-14, 16-20, 25 and 32-36 are not novel and do not involve an inventive step in the light of inventions disclosed in documents 1-3, cited in the international search report.

Document 1 discloses a method for measuring highdensity lipoprotein (HDL) cholesterol characterized in
that the specimen to be tested is reacted with cholesterol
ester hydrolase and (chemically modified) cholesterol
oxidase in an aqueous medium containing a bile acid
derivative having an anionic surfactant action (such as
dehydrocholic acid), and the hydrogen peroxide produced is
measured, and also discloses reagents (a kit) for
measuring high-density lipoprotein (HDL) cholesterol which
contain reagents used in said method of measurement, with

said reagents comprising a first reagent and a second reagent, wherein the cholesterol ester hydrolase and the bile acid derivative are contained in the first reagent, the cholesterol oxidase or cholesterol dehydrogenase is contained in the second reagent, and the reagent for measuring hydrogen peroxide is contained in the first reagent or the second reagent.

Therefore, the inventions set forth in claims 1, 3-7, 12-14, 16-20, 25 and 32-36 are substantially the same as the inventions disclosed in document 1.

2. Claims 2, 8-10, 15, 21-23, 26-31 and 37-39 do not involve an inventive step in the light in the light of inventions disclosed in documents 1-3, cited in the international search report.

Document 2 (see especially claims 1 and 6 and the section on background art in the detailed description of the invention) discloses reagents containing a bile acid or salt thereof, albumin, a non-ionic surfactant, cholesterol ester hydrolase, cholesterol oxidase and a reagent for measuring hydrogen peroxide, as reagents specific for the measurement of high-density lipoprotein (HDL) cholesterol (kit), and indicates that an anionic bile acid derivative such as taurocholic acid or glycocholic acid can be used as the bile acid; it also discloses a method for specific measurement of highdensity lipoprotein (HDL) cholesterol using said reagents wherein the cholesterol ester hydrolase, cholesterol oxidase and bile acid (derivative) are brought into contact with the specimen in the presence of albumin, and indicates that by this method, namely bringing the test specimen into contact with the enzymes in the presence of albumin, it is possible to inhibit reaction between the

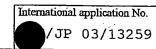
enzymes and LDL-cholesterol and VLDL-cholesterol in the specimen while reaction between the enzymes and HDL-cholesterol proceeds unimpeded.

It was well known in the art at the time of filing the present application that in general in order to measure high-density lipoprotein (HDL) cholesterol reliably, conditions in which there is as nearly as possible no reaction of the enzymes with LDL cholesterol and VLDL cholesterol present in the specimen (inhibition) are desirable.

Given this a person skilled in the art could easily conceive of applying the invention disclosed in document 2, and bring the enzymes and the specimen into contact in the presence of albumin, in the method for measuring high-density lipoprotein (HDL) cholesterol and measurement reagents (kit) for this purpose disclosed in document 1, applying the aforementioned commonly known fact so as to ensure the aforementioned conditions, namely to inhibit reaction between the enzymes and LDL-cholesterol and VLDL-cholesterol in the specimen, while allowing the reaction between the enzymes and HDL-cholesterol to proceed unimpeded, with the object of accurate measurement of HDL cholesterol.

In addition, document 3 discloses the possibility of using a compound represented by R1-CH2-CH(R2)-CH2-SO3- (R1 is a 3-(3-cholamidopropyl)dimethylammonio group and R2 is a hydrogen atom or a hydroxyl group) which acts as an amphoteric surfactant, as a bile acid derivative used in a specific method for measuring cholesterol.

Given this, using a compound represented by R1-CH2-CH(R2)-CH2-SO3- (R1 is a 3-(3-cholamidopropyl)dimethyl-ammonio group and R2 is a hydrogen atom or a hydroxyl group) which acts as an amphoteric surfactant, disclosed



in document 3 as a bile acid derivative used in a specific method for measuring cholesterol, in the method for measuring HDL-cholesterol and measurement reagents (kit) for this purpose disclosed in document 1, also does not involve any special difficulty.

3. The inventions set forth in claims 11, 24 and 40-42 are not disclosed in any of documents 1-4 above, cited in the international search report, and are novel and involve an inventive step.